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(FILE 'HOME' ENTERED AT 08:50:20 ON 31 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 08:50:31 ON 31 JUL 2002

L1 13304 S PROTEIN (2N) TYROSINE (2N) PHOSPHATASE
L2 1713 S L1 AND MUTANT
L3 0 S L2 AND TYR-46
L4 12 S L2 AND 46
L5 9 DUP REM L4 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 08:52:30 ON 31 JUL 2002

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 08:53:49 ON 31 JUL 2002

L6 625 S L1 AND PTP1B
L7 125 S L6 AND MUTANT
L8 0 S L7 AND 46
L9 12 S L6 AND 46
L10 5 DUP REM L9 (7 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 08:55:09 ON 31 JUL 2002

ANSWER 10 OF 13 CAPLUS COPYRIGHT 2002 ACS
AN 1998:106025 CAPLUS
DN 128:177559
TI **Substrate-trapping protein tyrosine phosphatase mutants** for identification of tyrosine-phosphorylated protein **substrates** and their clinical uses
IN Tonks, Nicholas; Flint, Andrew J.
PA Cold Spring Harbor Laboratory, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804712	A2	19980205	WO 1997-US13016	19970724
	W: CA, JP, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5912138	A	19990615	US 1996-685992	19960725
	CA 2262440	AA	19980205	CA 1997-2262440	19970724
	AU 9859395	A1	19990216	AU 1998-59395	19970724
	AU 728405	B2	20010111		
	EP 918867	A2	19990602	EP 1997-937017	19970724
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000515760	T2	20001128	JP 1998-508989	19970724
	US 5951979	A	19990914	US 1998-144925	19980901
PRAI	US 1996-685992	A	19960725		
	WO 1997-US13016	W	19970724		

AB Novel **protein tyrosine phosphatase mutants** that are catalytically attenuated are prepd. by replacing the invariant aspartate residue with an amino acid residue to reduce the Kcat to <1 min-1. The mutation does not cause significant alteration of Km. Also described are methods of (1) identifying tyrosine phosphorylated proteins which complex with the described **protein tyrosine phosphatase mutants**; (2) identifying agents that interfere the interaction between a PTP and a tyrosine phosphatase; (3) reducing the transforming effects of oncogenes or the formation of signaling complexes assocd. with p130cas; and (4) reducing cytotoxic effects assocd. with PTP. Prepn. and characterization of **PTP1B**[D181A], PTP-PEST[D199A], and PTP-PEST[C231S] are also described.

5 ANSWER 4 OF 9 MEDLINE DUPLICATE 1
AN 1999343735 MEDLINE
DN 99343735 PubMed ID: 10415025
TI Direct suppression of TCR-mediated activation of extracellular signal-regulated kinase by leukocyte **protein tyrosine phosphatase**, a tyrosine-specific phosphatase.
AU Oh-hora M; Ogata M; Mori Y; Adachi M; Imai K; Kosugi A; Hamaoka T
CS Biomedical Research Center, Osaka University Medical School, Japan.
SO JOURNAL OF IMMUNOLOGY, (1999 Aug 1) 163 (3) 1282-8.
Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199908
ED Entered STN: 19990820
Last Updated on STN: 19990820
Entered Medline: 19990812
AB Leukocyte **protein tyrosine phosphatase** (LC-PTP)/hemopoietic PTP is a human cytoplasmic PTP that is predominantly expressed in the hemopoietic cells. Recently, it was reported that hemopoietic PTP inhibited TCR-mediated signal transduction. However, the precise mechanism of the inhibition was not identified. Here we report that extracellular signal-regulated kinase (ERK) is the direct target of LC-PTP. LC-PTP dephosphorylated ERK2 in vitro. Expression of wild-type LC-PTP in 293T cells suppressed the phosphorylation of ERK2 by a **mutant** MEK1, which was constitutively active regardless of upstream activation signals. No suppression of the phosphorylation was observed by LC-PTPCS, a catalytically inactive **mutant**. In Jurkat cells, LC-PTP suppressed the ERK and p38 mitogen-activated protein kinase cascades. LC-PTP and LC-PTPCS made complexes with ERK1, ERK2, and p38alpha, but not with the gain-of-function sevenmaker ERK2 **mutant** (D321N). A small deletion (aa 1-**46**) in the N-terminal portion of LC-PTP or Arg to Ala substitutions at aa 41 and 42 resulted in the loss of ERK binding activity. These LC-PTP **mutants** revealed little inhibition of the ERK cascade activated by TCR cross-linking. On the other hand, the wild-type LC-PTP did not suppress the phosphorylation of sevenmaker ERK2 **mutant**. Thus, the complex formation of LC-PTP with ERK is the essential mechanism for the suppression. Taken collectively, these results indicate that LC-PTP suppresses mitogen-activated protein kinase directly in vivo.

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(FILE 'HOME' ENTERED AT 12:51:18 ON 30 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 13:08:39 ON 30 JUL 2002

L1 13542 S PROTEIN (3N) TYROSINE (3N) PHOSPHATASE
L2 115 S L1 AND SUBSTRATE AND TRAPPING AND MUTANT
L3 49 DUP REM L2 (66 DUPLICATES REMOVED)
L4 0 S L3 AND FLUORESE?
L5 5 S L3 AND FLUOR?

FILE 'STNGUIDE' ENTERED AT 13:11:59 ON 30 JUL 2002

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 13:15:09 ON 30 JUL 2002

L6 31 S L2 AND PTP1B
L7 13 DUP REM L6 (18 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:18:52 ON 30 JUL 2002

(FILE 'HOME' ENTERED AT 08:52:21 ON 29 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 08:52:28 ON 29 JUL 2002

L1	704	S PTP1B
L2	13295	S PROTEIN (2N) TYROSINE (2N) PHOSPHATASE
L3	624	S L1 AND L2
L4	1	S L3 AND FLUORESCEN? AND DETECT?
L5	125	S L3 AND MUTANT
L6	54	DUP REM L5 (71 DUPLICATES REMOVED)
L7	3	S L6 AND FLUORES?

FILE 'STNGUIDE' ENTERED AT 08:56:15 ON 29 JUL 2002

L7 ANSWER 2 OF 3 MEDLINE
AN 97203120 MEDLINE
DN 97203120 PubMed ID: 9050838
TI Development of "substrate-trapping" **mutants** to identify physiological substrates of **protein tyrosine phosphatases**.
AU Flint A J; Tiganis T; Barford D; Tonks N K
CS Cold Spring Harbor Laboratory, NY 11724, USA.
NC CA53840 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Mar 4) 94 (5) 1680-5.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
ED Entered STN: 19970422
Last Updated on STN: 20000303
Entered Medline: 19970407
AB The identification of substrates of **protein tyrosine phosphatases** (PTPs) is an essential step toward a complete understanding of the physiological function of members of this enzyme family. PTPs are defined by a conserved catalytic domain harboring 27 invariant residues. From a mutagenesis study of these invariant residues that was guided by our knowledge of the crystal structure of **PTP1B**, we have discovered a mutation of the invariant catalytic acid (Asp-181 in **PTP1B**) that converts an extremely active enzyme into a "substrate trap." Expression of this D181A **mutant** of **PTP1B** in COS and 293 cells results in an enzyme that competes with endogenous **PTP1B** for substrates and promotes the accumulation of phosphotyrosine primarily on the epidermal growth factor (EGF) receptor as well as on proteins of 120, 80, and 70 kDa. The association between the D181A **mutant** of **PTP1B** and these substrates was sufficiently stable to allow isolation of the complex by immunoprecipitation. As predicted for an interaction between the substrate-binding site of **PTP1B** and its substrates, the complex is disrupted by vanadate and, for the EGF receptor, the interaction absolutely requires receptor autophosphorylation. Furthermore, from immunofluorescence studies, the D181A **mutant** of **PTP1B** appeared to retain the endogenous EGF receptor in an intracellular complex. These results suggest that the EGF receptor is a bona fide substrate for **PTP1B** in vivo and that one important function of **PTP1B** is to prevent the inappropriate, ligand-independent, activation of newly synthesized EGF receptor in the endoplasmic reticulum.
This essential catalytic aspartate residue is present in all PTPs and has structurally equivalent counterparts in the dual-specificity phosphatases and the low molecular weight PTPs. Therefore we anticipate that this method may be widely applicable to facilitate the identification of substrates of other members of this enzyme family.

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2001:661648 CAPLUS
DN 135:207456
TI Obtaining inhibitors/activators of an enzyme by using an inactive **mutant** enzyme that binds substrate and a protein-protein interaction screening system and pharmacological applications

IN Liu, Yi; Wang, Shaojie; Zhang, Zhong-yin
PA Morphochem A.-G., Germany
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001064939	A2	20010907	WO 2001-EP2438	20010302

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-517170 A 20000302

AB The invention relates to a generally applicable process for obtaining inhibitors/activators of an enzyme by using an enzymically inactive **mutant** enzyme that binds substrate and a protein-protein interaction screening system, such as a **fluorescence** polarization based assay. Preferably the enzyme is a **protein tyrosine phosphatase**, a **protein tyrosine** kinase, a protease, a Ras protein, or a Raf protein. A **fluorescence** polarization based assay for human **protein tyrosine phosphatase** 1B inhibitors using C215S **mutant** of **PTP1B**, and a **fluorescein** labeled phosphotyrosine peptide as peptide substrate is disclosed. The obtained inhibitors/activators can be used for the prepn. of medicaments for treating diseases caused by or involved with the activity of the enzyme. The **PTP1B** inhibitor can be used for treating diabetes or obesity.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	21.20	21.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.62	-0.62

FILE 'STNGUIDE' ENTERED AT 08:56:15 ON 29 JUL 2002

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jul 26, 2002 (20020726/UP).

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments
1	BRS	L1	868	protein near2 tyrosine near2 phosphatase	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/31 08:41	
2	BRS	L8	275	l1 and substrate and mutant	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/31 08:34	
3	BRS	L15	130	l8 and (fluorescein or rhodamine or alexafluor or bodipy)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/31 08:35	
4	BRS	L22	130	l15 and activity	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/31 08:35	

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments
5	BRS	L29	10	l22 and trapping	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/31 08:36	
6	BRS	L36	3	l1 and tyr-46	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/31 08:44	
7	BRS	L43	398	l1 and "46"	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/31 08:44	